

ATTACHMENT 10

PCT

WORLD INTELLECTUAL PROPERTY
International



INTERNATIONAL APPLICATION PUBLISHED UNDE

WO 9604933A2

<p>(51) International Patent Classification ⁶ : A61K 39/395, A23K 1/00</p>		<p>A2</p>	<p>(11) International Publication Number: WO 96/04933 (43) International Publication Date: 22 February 1996 (22.02.96)</p>
(21) International Application Number:	PCT/US95/09227	(81) Designated States:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).
(22) International Filing Date:	21 July 1995 (21.07.95)	Published	<i>Without international search report and to be republished upon receipt of that report.</i>
(30) Priority Data:	08/286,376 5 August 1994 (05.08.94) US		
(71) Applicant:	WISCONSIN ALUMNI RESEARCH FOUNDATION [US/US]; 614 North Walnut Street, Madison, WI 53705 (US).		
(72) Inventors:	COOK, Mark, E.; 313 S. Segoe Road, Madison, WI 53705 (US). MILLER, Cheryl, C.; 2610 McKenna Boulevard, Madison, WI 53711 (US). PIMENTEL, Julio, L.; 3206 Windgate Drive, Buford, GA 30519 (US).		
(74) Agent:	WOZNY, Thomas, M.; Andrus, Sceales, Starke & Sawall, Suite 1100, 100 East Wisconsin Avenue, Milwaukee, WI 53202 (US).		
(54) Title:	CCK ANTIBODIES USED TO IMPROVE FEED EFFICIENCY		
(57) Abstract	<p>A method of increasing food efficiency in both avians and mammals by using antibodies to cholecystokinin to elicit a biological response which decreases gastrointestinal motility, reduces satiety and improves feed efficiency.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

**CCK ANTIBODIES USED TO IMPROVE
FEED EFFICIENCY**

Field of the Invention

This invention relates to eliciting biological response in
5 mammals or poultry either by passive transfer of an antibody or
upon feeding an antibody containing substance to the animal.
Specifically, this invention relates to increasing food efficiency,
decreasing gastrointestinal motility and decreasing satiety in
10 animals and humans by the use of antibodies to cholecystokinin
(CCK).

Background of the Invention

The immune system, based on several kinds of specialized
blood white cells, is a highly specific defense system that
recognizes, eliminates and remembers foreign macromolecules and
15 cells. While functioning properly, it can distinguish between "self"
and "non-self" (foreign) materials. For example, it views tumor
cells as non-self and hence attacks them, protecting animals
against cancer-causing tumor cells as it protects against other
invading macromolecules.

20 An antigen is a foreign substance that when introduced into
an animal with a functioning immune system, can elicit a specific
immune response such as the one mentioned above. Once activated
the immune response involves, among other things, production of
antibodies in the circulation system specific to that antigen. There
25 are five distinct classes of antibodies which are also called
immunoglobulins. The most abundant is IgG. The other four are
IgM, IgA, IgD, and IgE. These antibodies combine with the antigen
and act to neutralize or counter the effects of the antigen
introduced into the animal. They accomplish this result by binding
30 to the antigen thereby neutralizing it and preventing it from
binding to other specific cell receptors.

- 2 -

The immune system can be used not only to fight off pathogenic antigens or harmful foreign molecules, but can be manipulated in order to elicit favorable responses which are not naturally occurring. For example, naturally occurring proteins in an animal can be neutralized via introduction of antibodies specific to that protein thereby neutralizing that protein's normal physiological affect on the animal's system.

There are several ways in which an animal becomes immune responsive. For example, some antibodies are able to traverse the placenta from a mother's circulation to that of her fetus. As a result, the progeny of that mother receives natural immune protection by "inheriting" the mother's own antibodies before birth.

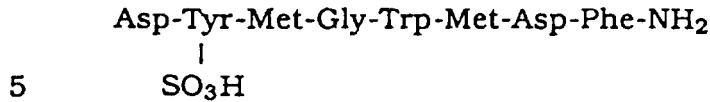
A second way to elicit an immune response is through introduction of an antigen into one animal, resulting in that animal developing specific antibodies to that antigen. These antibodies can then be isolated from the animal and introduced into a second animal resulting in the second animal having antibody that can bind the specific antigen.

Summary of the Invention

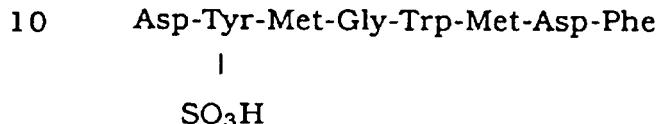
This invention pertains to eliciting an immune response in animals and humans in order to increase food efficiency. The antibody used in this invention is an antibody specific to the peptide cholecystokinin (CCK). The cholecystokinin antibody (CCK antibody), upon introduction to the animal, causes an increased efficiency of converting food to body weight gain and through an apparent decreased gastrointestinal motility thereby increasing food efficiency.

- 3 -

The CCK peptide is as follows:



The CCK peptide can also be in a non-amide form:



15 CCK is an octapeptide that has been shown to negatively affect food intake and thus inhibit growth in both mammals (Gibbs et al, 1973) and birds (Savory and Hodgkiss, 1984). CCK antibodies have been successfully produced endogenously in pigs (Pekas and Trout, 1990; Pekas 1991) and rats (MacLaughlin et al, 1985). In both species, the adverse effects of CCK on food intake and weight gain were prevented by endogenous circulation of CCK antibodies.
20

The effects of CCK in domestic fowls is well known (Savory et al, 1981). CCK represents a polypeptide hormone which is released when food enters the small intestine. The presence of CCK in the gut mucosa alters gastrointestinal (GI) motility. The gizzard controls the rate in which food travels through the intestine and CCK, which is normally released after a meal is consumed, causes a decrease in gizzard contraction and an increase in intestinal contraction. This results in less time for the absorption of food and nutrients in the intestinal tract. The inventors have found that transferring CCK antibody to poultry increases feed efficiency. In other words, the birds gain more weight per pound of food.

- 4 -

The presence of CCK also alters the willingness to eat. CCK is responsible for what is known as the satiety effect which is a physiological effect that sharply decreases an avian's appetite. If an antibody combines with CCK, CCK is neutralized, the satiety effect 5 is inhibited and adverse effects of endogenous CCK on gastrointestinal motility is averted. Thus, the avian gains more weight per unit of intake. It has not previously been seen that CCK antibodies function in avians or function orally and are actually able to neutralize the negative affects of CCK.

10 Neuropeptide Y and bombesin have similar physiological effects to CCK on mammalian systems and avian systems. These neuropeptides are also found in the gut and alter feeding behavior.

15 The effect of CCK antibodies on food efficiency and weight gain can be achieved by (1) passively transferring the CCK antibodies from the dam to offspring, (e.g. by injecting the breeder hen such that the offspring have increase levels of CCK antibody); (2) by feeding a yolk product high in CCK antibody directly to the animal; or (3) injecting a substance high in CCK antibody directly to the animal.

20 The method in which an immune response is achieved passively involves inoculating a female avian with a specific antigen which results in passively transferring the antibody to the female's offspring. This passive transfer of antibodies to CCK from the dam to the progeny resulting in improved conversion of food into body 25 weight has not previously been seen in the art.

30 This invention also relates to a specific antibody containing substance produced from the egg of a hen immunized against a selected antigen wherein the substance is mixed with feed and subsequently fed to poultry to elicit altered but improved physiological response. Antibodies to CCK can be produced in

- 5 -

laying hens, passed to the yolk, harvested from the yolk or fed as dried yolk, and used as a feed additive for improving feed efficiency in poultry has also not been previously appreciated in the art.

5 This invention has many advantages. One advantage is that individuals in the commercial meat industry can achieve market weight in livestock or poultry using less time and less feed thereby drastically reducing costs.

10 A second advantage to the present invention is that the CCK antibodies neutralize CCK but have no known harmful side affects and do not appear to affect meat quality. Also, the cost of utilizing this invention, even on a large scale, is relatively low since only .1 to 1 CCK antibody-containing egg is required per eight pounds of feed.

15 In addition, using the method of feeding the antibody to domesticated animals is relatively low in labor costs since the antibody can simply be mixed with feed and thus, not every individual animal must be injected with the antibody. Also, there is no need to separate or isolate the antibody from the egg since whole egg or yolk can simply be spray dried and fed directly.

20 Another advantage of this invention is that it counteracts the negative affect of feeding raw soybean meal to poultry or livestock. For example, a typical chick diet contains 40% soybean meal. However, raw soybean meal cannot be fed to poultry because it contains trypsin inhibitor which inhibits the ability of trypsin to 25 digest protein. Therefore, raw soybean meal causes increased levels of CCK with a concurrent decrease in feed efficiency. In order to counter this effect, soybeans must be heat treated in order to be fed to poultry. The typical process for preparing soybean involves heating the beans, extracting the oils and using the 30 remaining meal for chick feed. Specifically, the beans must be heated to at least 121°C for approximately 20-40 minutes. There

- 6 -

are several problems associated with preparing soybeans for poultry feed. One is that the heating process must be performed at an extremely high temperature to ensure destruction of the trypsin inhibition factor. Secondly, heating has a negative impact on the 5 quality of proteins in the soy meal and makes the denatured protein difficult to digest properly. However, the inventors have found that CCK antibodies protect against the negative effects of feeding raw soybeans to fowl.

In addition to soybean, there are a number of other plants 10 that contain trypsin inhibitor, including wheat, barley, lima beans and various legumes. It is predicted that the CCK antibody will also protect against the negative affects of feeding products made from wheat, barley, lima bean or legumes to poultry or livestock.

This invention also has many advantages over what is 15 currently being used in the poultry and livestock industries. Antibiotics are currently used in the commercial animal industry in order to increase food efficiency and weight gain. However, antibiotics leave a drug residue in the animal's tissue. Therefore, the animal must go through "withdrawal time". Withdrawal time is 20 an amount of time sufficient for the antibiotic to clear animal tissues. During withdrawal time, the animal cannot be slaughtered for human consumption. Additionally, any eggs or milk produced cannot be utilized for human use. This precaution is utilized because of the concern that human consumption of milk with 25 traces of penicillin, for example, will cause increase resistance to antibiotics in man, eventually rendering the use of antibiotics to fight bacterial diseases useless.

- 7 -

Secondly, the use of antibiotics over a long period of time can potentially cause an increased number of microorganisms able to infect an animal because these organisms slowly gain resistance due to constant exposure to the antibiotic. Thus, future bacterial 5 diseases will be difficult if not impossible to treat.

CCK also has the same effects of increased GI motility and satiety inhibition in mammals (Pekas and Trout, 1990). It is a well known fact that mammalian species passively transfer antibodies to their progeny as do avians and that mammals respond to CCK 10 autoimmunization as do avians. The dam's antibodies are also identical to those passively transferred to the progeny in avians as well as mammals. Similarly, feeding raw soybean exerts analogous increases in CCK production in mammals as it does in birds (Weller et al, 1990; Chohen et al, 1993; Can J An Sci 73; 401). Therefore, 15 based on the aforementioned facts, the protective effects of actively fed and passively transferred CCK antibodies against satiety and poor feed conversion resulting from CCK observed in avians would also be seen in mammals. Using CCK on various livestock such as cattle and swine would drastically increase their final 20 weight using the same amount of animal meal. Thus the costs to produce an animal of market size is decreased and this would have an enormously beneficial effect on the livestock industry.

The invention would be highly beneficial to humans who are underweight or have problems maintaining their weight. 25 Additionally, individuals with eating disorders would benefit from this invention because their food intake could be controlled.

As previously stated, there are other gastrointestinal peptides or hormones which have an effect on an animal's feeding behavior and digestion. The example of CCK and the method of 30 using CCK antibodies directed toward that peptide in order to prevent CCK's adverse effects suggests that similar responses could

- 8 -

be achieved using other antibodies specific to gastrointestinal peptides or hormones. For example, gastrin is involved in signaling acid secretion into the gut and has a trophic action on gastric mucosa leading to hyperplasia. An antibody to gastrin could be used
5 to decrease acid secretion in animals with gastric ulcers or in cases where there is gastric ELC cell carcinoid tumors due to prolonged hypergastrinemia. Gut somatostatin inhibits food intake in fed animals as well as many other gut activities. An antibody to somatostatin could prevent its inhibitory activities. Bombesin
10 stimulates a release of CCK. One could hypothesize that inhibiting bombesin using an antibody specific to bombesin may result in responses similar to antibodies specific to CCK. Neuropeptide Y has been reported to be a stimulus in feeding. It may be possible to inhibit its activity and regulate obesity in animals prone to develop
15 such problems. The biological activity of other peptides which regulate intestinal motility and other functional properties of the intestine could be regulated using the technology described.

In general, by generating antibodies to peptides, hormones, cytokines, etc. that regulate biochemical, metabolic, physiological,
20 and/or behavioral processes, it may be possible to regulate or alter an animal's system to compensate for a physical abnormality or accentuate a normal function.

Detailed Description of the Preferred Embodiment

As previously mentioned, there are three modes in eliciting
25 an immune response to CCK in mammals or poultry: passive transfer, active feeding, and active inoculation.

The mode of this invention which relates to passively transferring antibodies involves injecting laying hens with CCK wherein the hens produce antibodies specific to CCK and, as a
30 result, those antibodies are then passively transferred into the egg yolk of eggs laid by the hens. The chick embryo absorbs the CCK

- 9 -

antibody during embryonic development. Thereafter, the CCK antibodies become circulating in the hatched chick's bloodstream as well as passed to the gastrointestinal tract.

Either purified CCK or synthesized CCK peptide can be used. Well known means in the art can be used for purifying the CCK peptide such as fractionization, chromatography, precipitation or extraction. However, CCK should be conjugated with a carrier or foreign protein for use as the antigen. CCK alone has a molecular weight less than 1,500 Daltons. In order to invoke an immune response, a molecular weight of at least 10,000 Daltons is required. Therefore, the CCK peptide should be conjugated with a carrier protein with a molecular weight of approximately 8,000 Daltons or more in order for the conjugate to elicit an immune response. Carriers include a wide variety of conventionally known substances but commonly entail bovine gamma globulin or keyhole limpet hemocyanin.

The CCK peptide conjugated to its carrier protein is injected into the target animal with a common adjuvant. The CCK-carrier conjugate can be emulsified in Freund's complete adjuvant, for example. If mammals are the target animals, then subsequent inoculations should consist of incomplete adjuvant.

Another mode of this invention involves orally feeding a CCK antibody containing substance produced from eggs of a CCK vaccinated hen. The CCK antibody containing eggs are prepared and mixed into animal meal. Poultry or mammals which consume this antibody containing meal soon show beneficial response by preventing the satiety effects specific to CCK.

The production of CCK antibody for oral administration can be done by utilizing known technology for producing antibodies in egg yolks. In that process, hens are challenged by injecting them with CCK conjugated to a carrier protein. In response to exposure

- 10 -

to the CCK antigen, the eggs laid by these hens contain high levels of CCK antibody in the yolk. Automated systems then separate and spray dry the yolks into a powder. The yolks can alternatively be lyophilized. This standard technique is well established in the art
5 for producing various antibodies for other purposes (e.g. diagnoses, resistance to pathogens, etc.)

Whole eggs may be used and it is therefore not necessary to separate the yolk from the albumen. Typically, .1 to 1 CCK containing egg is used per 8 pounds of feed.

10 Chickens are the most preferable source of eggs but eggs from turkeys, geese, ducks and the like may also be used.

While eggs are the logical source of massive quantities of antibodies, it is possible to collect the antibodies from whole blood, plasma or serum when chickens are processed for meat. In
15 addition, whole blood, plasma or serum from inoculated livestock may be another source of antibodies as well as milk derived from an inoculated cow or goat. Additionally, another source of antibody production is through cell fusion using hybridoma techniques, genetically altered cell cultures or fermentation using recombinant
20 technology.

A third mode of this invention is via inoculation. CCK antibodies can be directly injected into a target animal in order to elicit the desired response of satiety and improved feed conversion.

The target animal receiving the CCK antibody varies greatly.
25 Commercial animals such as livestock, poultry and pelt-animals (e.g. mink, sable, etc.) are ideal candidates. Additionally, humans who have difficulty gaining weight are also considered within the scope of this invention.

- 11 -

PASSIVELY TRANSFERRED CCK ANTIBODIES ON
PERFORMANCE OF YOUNG LEGHORN CHICKS.

Example 1

Methods

5 Cholecystokinin (CCK-8) (Fragment 26-33 amide with sulfated tyrosine) was conjugated to keyhole limpet hemocyanin (KLH) using glutaraldehyde and was emulsified with Freund's complete adjuvant (1:1) and injected (100ug CCK) into 11 Single Comb White Leghorn laying hens. A second injection of the CCK-8 conjugate in Freund's incomplete adjuvant was injected 7 days after primary injection. Another group of control hens which did not receive the CCK injection were also used. Hens (control and CCK injected) were fertilized (artificially using semen collected from New Hampshire roosters). Fertile eggs collected 5 months after 10 the initial injection were used to determine chick performance as a result of passively transferred CCK antibodies. Fifteen chicks hatched from the control hens and 15 chicks hatched from the CCK injected hens were raised in battery brooders on corn-soybean meal based diets for 6 weeks. Body weight gain and feed 15 consumption data were collected.

Results

20 Chicks from CCK injected hens had improved feed conversion (less feed per pound of gain) which was 14% better than chicks from the control hens. Also, feed intake was increased 25 in CCK birds. The results are shown as Table I.

TABLE I

Antibody Treatment	6 Week Gain*		6 Week Intake*		6 Week Conversion	
	Change	%	Change	%	Change	%
Control	297		745		2.51	
CCK	352	+18	756	+1	2.15	-14

30 *Body weight, body wt gain and feed intake are measured in grams.

- 12 -

Example 2

Methods

Eggs from hens immunized with CCK (as shown in Example 1) and from control hens were collected at approximately 10 months after the primary inoculation. Two pens of 13 chicks (representing both the control and CCK immunized hens) were fed a corn-soybean meal based diet to determine if passively transferred CCK antibodies would influence performance as seen in Example 1. Birds were raised for 4 weeks. Body weights and feed consumption were determined.

Results

Feed conversion was improved 2% in chicks from CCK immunized hens when compared to chicks from control hens. The results are shown as Table II.

15

TABLE II

Treatment	4 Week		4 Week		4 Week	
	Weight*	% Change	Intake*	% Change	Conversion	% Change
Control	158		383		2.42	
CCK	151	-4	360	-6	2.38	-2

*Body weight, body wt gain and feed intake are measured in grams.

Example 3

Methods

25 Fertile eggs were collected approximately 8 months after primary inoculation from control and CCK injected hens (immunization as described in Example 1) and used to study the effects of CCK immunization on progeny performance. Two pens of 17 progeny chicks per pen from CCK injected hens and 2 pens of 17 progeny chicks per pen from control hens were raised for 4 weeks. Body weight and feed consumption were measured.

30

- 13 -

Results

Chicks from CCK injected hens had a 5.2% improvement in feed conversion than chicks from control hens. The results are shown as Table III.

5

TABLE III

	4 Week	4 %	4 Week	4 %	4 Week	4 %	
	<u>Treatment</u>	<u>Weight*</u>	<u>Change</u>	<u>Intake*</u>	<u>Change</u>	<u>Conversion</u>	<u>Change</u>
10	Control	246		473		1.92	
	CCK	245	0	447	-5.5	1.82	-5.2

*Body weight, body wt gain and feed intake are measured in grams.

Example 4

Methods

15 In this study, 2 pens of 15 chicks per pen from CCK immunized hens (as shown in Example 1 and 7 months following the hen's primary inoculation) and 2 pens of 12 chicks per pen from control hens were raised on a corn-soybean meal based diet supplemented with 5% raw soybeans for 3 weeks (raw soybeans were used to stimulate CCK production). Body weight and feed 20 consumption were measured.

Results

Chicks from CCK injected hens had a 10% improvement in feed conversion when compared to chicks from control hens. The results are shown in Table IV.

25

TABLE IV

	3 Week	3 %	3 Week	3 %	3 Week	3 %	
	<u>Treatment</u>	<u>Weight*</u>	<u>Change</u>	<u>Intake*</u>	<u>Change</u>	<u>Conversion</u>	<u>Change</u>
30	Control	169		395		2.34	
	CCK	161	-5	338	-14	2.10	-10

*Body weight, body wt gain and feed intake are measured in grams.

5

**PROTOCOL FOR THE EFFECTS OF PASSIVELY
TRANSFERRED CCK ANTIBODY ON THE PERFORMANCE
OF YOUNG BROILER CHICKS.**

Example 5

Methods

Broiler breeders were immunized with CCK conjugated to KLH using the protocol described in example 1. Since these breeders were maintained on the floor, fertile eggs were produced as a result of natural matings. A total of 10 hens received the CCK immunization (antigen prepared as in example 1 for Leghorns), and 10 hens served as controls. Approximately 21 to 30 days after the primary inoculation, fertile eggs were collected from the control and CCK immunized hens. Seven broiler chicks from the control hens and 7 broiler chicks from the CCK injected hens were hatched and raised in a battery brooder for 3 weeks. Body weight and feed consumption were measured.

15

Results

20

Feed conversion was improved 20% and body weight 8% in broiler chicks from CCK immunized hens as compared to broiler chicks from control hens. See Table V for results.

TABLE V

Treatment	3 Week		3 Week		3 Week	
	Weight*	% Change	Intake*	% Change	Conversion	% Change
Control	396		604		1.53	
CCK	427	+8	526	-13	1.23	-20

*Body weight, body wt gain and feed intake are measured in grams.

30

Example 6

Methods

Two pens of 6 chicks from CCK immunized broiler breeders 7 weeks after the primary inoculation as in Example 5 and 2 pens

- 15 -

of 6 chicks per pen from the control hens were hatched and raised to 3 weeks of age on a standard broiler type diet. Body weight and feed consumption were measured.

Results

5 Broiler chicks from CCK immunized hens gained 16% more body weight and converted food 12.5% more efficiently than chicks from the control hens. See Table VI for results.

TABLE VI

10	<u>Treatment</u>	3		3		3	
		Week	%	Week	%	Week	%
	Control	380		547		1.44	
	CCK	441	+16	547	0	1.26	-12.5

*Body weight, body wt gain and feed intake are measured in grams.

15

**FEEDING EGG YOLKS FROM CONTROL AND CCK
IMMUNIZED HENS.**

Example 7

Methods

20

Control or CCK immunized hens were prepared as described in Example 1. Eggs from control and CCK immunized hens were collected after at least 21 days following the primary inoculation. Yolks were collected from the eggs (albumen was discarded) and control or anti-CCK yolks were separately pooled, frozen, then freeze dried. The control and CCK antibody dried yolks were then ground and added to a standard corn-soybean based diet at .5, 1.0, or 5% of the diet (weight by weight) creating 3 control treatments and 3 anti-CCK treatments. Each dietary treatment was fed to two pens of 9 leghorn type chicks for 4 weeks. Body weight gains, feed consumption, and feed conversion were determined.

30

- 16 -

Results

As the level of anti-CCK egg yolk increased, body weight gain increased relative to those fed the control egg yolk. At each level of anti-CCK egg yolk feeding, feed conversion was improved over 5 those fed the control yolk. See Table VII for results.

TABLE VII

-----0-4 weeks of age-----

<u>Treatment</u>	<u>% Fed</u>	<u>Feed Intake*</u>	<u>Feed Conversion</u>
Control Yolk	.5	692	2.88
CCK Yolk	.5	680	2.50
Control Yolk	1.0	656	2.39
CCK Yolk	1.0	649	2.29
Control Yolk	5	712	2.55
CCK Yolk	5	772	2.49

15 *Body weight, body wt gain and feed intake are measured in grams.

**EFFECTS OF PASSIVELY TRANSFERRING CCK ANTIBODY
IN PREVENTING THE NEGATIVE EFFECTS OF FEEDING
RAW SOYBEANS ON FEED CONVERSION.**

20 Example 8

Methods

Immunized hens (Leghorns) were prepared as described in Example 1. Hens were artificially fertilized and eggs were collected and incubated. Chicks (Single Comb White Leghorn X 25 New Hampshire) were hatched and 2 pens of 12 chicks were assigned to each of 4 treatments. The treatments included 2 sources of chicks (progeny from control or CCK immunized hens) factorially arranged with 2 dietary treatments (5 or 10% raw soybeans at the expense of diet). The chicks were fed the diets for 30 4 weeks and body weight and feed consumption were measured.

- 17 -

Results

Chicks from CCK immunized hens had improved feed conversion (11% to 19%) when compared to their respective control diets. As the level of raw soybeans increased in the diet, 5 feed conversion was poorer (12% poorer in the control progeny, but only 6% poorer in the progeny chicks from the CCK injected hens). See Table VIII for results.

TABLE VIII

	<u>% Raw Soybean</u>	<u>Passive CCK Antibody</u>	<u>4 Week Weight*</u>	<u>% Change</u>	<u>4 Week Conversion</u>	<u>% Change</u>
10	5	-	202		2.63	
	5	+	205	+1.5	2.34	-11
	10	-	192		2.94	
15	10	+	197	+2.6	2.48	-19

*Body weight, body wt gain and feed intake are measured in grams.

- 18 -

We claim:

1. A method of transferring cholecystokinin (CCK) antibodies to an animal in order to increase food efficiency and decrease intestinal motility:

5 administering to said animal a CCK antibody containing substance wherein said substance is derived from a producer animal wherein said producer animal has been immunized with a cholecystokinin peptide.

2. The method of claim 1 wherein said administering is via inoculation.

3. The method of claim 1 wherein said administering is via feeding.

4. The method of claim 1 wherein said animal is an avian.

5. The method of claim 4 wherein said avian is a domesticated fowl.

6. The method of claim 1 wherein said animal is a mammal.

7. The method of claim 1 wherein said producer animal is selected from a porcine, bovid, ovine, or caprine.

8. The method of claim 1 wherein said substance is derived from a by-product of said producer animal.

9. The method of claim 8 wherein said by-product is selected from whole blood, serum, plasma or milk.

10. The method of claim 1 wherein said producer animal is a female avian.

11. The method of claim 10 wherein said female avian is a domesticated fowl.

- 19 -

12. The method of claim 10 wherein said substance is derived from whole egg.

13. The method of claim 10 wherein said substance is derived from egg yolk.

14. The method of claim 1 wherein said CCK is purified CCK peptide.

15. The method of claim 1 wherein said CCK is synthetic CCK peptide.

16. The method of claim 1 wherein said CCK is sulfated.

17. The method of claim 1 wherein said CCK is non-sulfated.

18. The method of claim 1 wherein said CCK is an amide.

19. The method of claim 1 wherein said CCK is conjugated to a carrier protein.

20. The method of claim 19 wherein said carrier protein is keyhole limpet hemocyanin.

21. The method of claim 19 wherein said carrier protein is bovine gamma globulin.

22. The method of claim 19 wherein said CCK conjugated to said carrier protein has a molecular weight of at least 8,000 Daltons.

23. The method of claim 6 wherein said domesticated fowl is a chicken.

24. The method of claim 7 wherein said mammal is a rodentia.

25. The method of claim 7 wherein said mammal is a homo sapien.

26. The method of claim 7 wherein said mammal is a domesticated mammal.

27. The method of claim 7 wherein said domesticated mammal is selected from a porcine, bovid, ovine, or caprine.

- 20 -

28. A method of transferring cholecystokinin (CCK) antibodies in animals in order to increase food efficiency and decrease intestinal motility:

5 immunizing an animal with CCK so that said animal produce antibodies to CCK and passively transfer said antibodies to said animal's progeny whereby said progeny show an immune response of increased food efficiency and decreased intestinal motility.

29 The method of claim 28 wherein said animal is an avian.

30. The method of claim 28 wherein said animal is a mammal.

31. The method of claim 29 wherein said avian is a domesticated fowl.

32. The method of claim 31 wherein said domesticated fowl is a chicken.

33. The method of claim 28 wherein said CCK is conjugated to a carrier protein.

34. The method of claim 33 wherein the carrier protein is keyhole limpet hemocyanin.

35. The method of claim 33 wherein the carrier protein is bovine gamma globulin.

36. The method of claim 33 wherein the CCK conjugated to the carrier protein has a molecular weight of at least 8,000 Daltons.

37. The method of claim 30 wherein said mammal is a rodentia.

38. The method of claim 30 wherein said mammal is a homosapien.

39. The method of claim 30 wherein said mammal is a domesticated mammal.

40. The method of claim 39 wherein said domesticated mammal is selected from a porcine, bovid, ovine, or caprine.

- 21 -

41. A feed substance for an animal, comprising:
an organic meal; and
an effective amount of antibodies which bind with CCK.

42. The feed of claim 41 wherein said antibodies are derived
from eggs of immunized avians.

43. The feed of claim 41 wherein said animal is a
domesticated animal.

44. The invention of claim 43 wherein said domesticated
animal is a fowl.

45. The feed claim of claim 44 wherein said fowl is a
chicken.

46. The feed of claim 43 wherein said domesticated animal
is a mammal.

47. The feed of claim 46 wherein said mammal is selected
from a porcine, bovid, ovine, or caprine.

48. A method of countering the negative effects of trypsin
inhibitor when feeding plant material containing trypsin inhibitor
to animals comprising:

5 feeding said animals a meal wherein said meal contains an
effective amount of CCK antibody.

49. The method of claim 48 wherein said plant material is
soybean.

50. A method of transferring gut peptide antibodies to an
animal which negates the physiological effect of said peptide:

5 administering to said animal an antibody specific to a gut
peptide wherein said gut peptide is derived from a producer animal
wherein said producer animal has been immunized with a gut
peptide.

51. The method of claim 50 wherein said gut peptide is
selected from bombesin, neuropeptide Y, gastrin or somatostatin.

- 22 -

52. A method of transferring gut peptide antibodies in animals in order to increase food efficiency and decrease satiety comprising:

5 immunizing an animal with a gut peptide so that said animal produce antibodies to said gut peptide and passively transfer said antibodies to said animal's progeny which negates the physiological effect of said peptide.

53. The method of claim 52 wherein said gut peptide is selected from bombesin, neuropeptide Y, gastrin or somatostatin.

54. A method of transferring antibodies to an animal in order to modify a biochemical process comprising:

5 administering to said animal an antibody containing substance wherein said substance is derived from a producer animal wherein said producer animal has been immunized with an antigen wherein said antigen regulates a biochemical process.